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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,559	04/08/2004	Clark Pan	AERO1210-2	9562

7590 07/27/2007

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	**PAPER NUMBER**
1647	

MAIL DATE	DELIVERY MODE
07/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,559	PAN ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-12,18,22,25-27,30-35,37,43-50,56 and 63-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-12,18,22,25-27,30-35,37,43-50,56,63 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Applicant's Amendment:

1a. Applicants' amendment filed on 17 April 2007 has been entered.

Status of Claims

1b. Claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 56, 63-64 are pending and under consideration in the instant application.

Response to Applicant's Argument:

2. The following rejections are withdrawn in light of Applicant's arguments:

2a. All of the objections and rejections of cancelled claims are moot.

2b. The objection of claims 43-50 and 56 for depending from non-elected claims is withdraw, because Applicants have corrected the dependency of said claims.

2c. The rejection of claims 5-14, 18, 31, 32, 33, 34, 35, 43-50, made under U.S.C. §112, first paragraph, as not enabling the full scope of the claimed invention is withdrawn, because the claims are now drawn to a specific IL-4 muteins that are fully enabled.

2d. The rejection of claims 5, 6, 12, 13, 22, 26, 28, 30, 60, 62-64 and 43-44, 50-52, made under U35 U.S.C. 102(b) as being anticipated by Wild et al U.S. Patent 6,130,318, 10 October 2000 is withdrawn, because Wild et al do not disclose an IL-4 mutein receptor antagonist wherein the amino acid at residue 37, 38 or 104 is a cysteine residue. Wild et al. describe PEGylation of aspartic acid residues at positions 38 and 105 and not PEGylation of cysteine residues as 37, 38 or 104 as claimed.

2e. The rejection of claims 5-7, 14, 7, 22-30, 36 made under 35 U.S.C. 103(a) as being unpatentable over Wild et al U.S. Patent 6,130,318, 10 October 2000 in view of Kreitman et al (1994), is withdrawn, because neither Wild et al nor Kreitman et al provide motivation to replace amino acid at residue 37, 38 or 104 of IL-4 with a cysteine residue to PEGylate said IL-4 mutein.

New Rejections:

Claim Rejections - 35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 53, 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox III, et al (U.S. Patent 6,608,183, 19 August 2003) in view of Wild et al (U.S. Patent 6,130,318, 10 October 2000)

The instant claims 5-12, 18, 22, 25-27, 30-35, 37, 43-50, 53, 63-64, encompass modified IL-4 mutein receptor antagonists that bind to the IL-4 receptor, wherein amino acid residue 37, 38 or 104 is a cysteine residue, wherein said mutein is coupled to non-

protein polymers, (polyethylene glycol, polypropylene glycol or polyoxyalkylenes) said muteins produced by culturing a host cell comprising polynucleotide of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

Cox et al disclose mutants of the growth hormone family, wherein specific amino acids are substituted with the amino acid cysteine, using site directed mutagensis, then covalently coupling a polymer via the cysteine residue, (column_2, lines 29-43, column 36, lines 15-40). Cox et al also disclose that modification of the proteins (such as IL-4) by linking it to non-protein polymers, such as polyethelyne glycol, polypropylene glycol via the cysteine residue, significantly improves the half-life of the protein in the body, (see column column 3, liens 48-67). The muteins disclosed by Cox et al retain the desired activity and are partially reduced with dithiothreitol (DTT) in order to achieve optimal PEGylation of the free cysteine, (see column 21, lines 37-67). However, Cox et al do not teach modified IL4 muteins, wherein the specific amino acids 37, 38 or 104 are cysteine or wherein said IL-4 muteins are antagonists that inhibit IL-4 mediated processes.

Wild et al disclose several human IL-4 mutant proteins, in which specific amino acids residues are modified to generate antagonists of IL-4, for example where residues at position 38 and 105 are modified, (see abstract and column 3, lines 35-50). Wild et al also disclose IL-4 mutant antagonists that inhibit IL-4 mediated processes, (see column 8, lines 15-20). Also taught are recombinant materials for making such a fusion protein, expression vectors, see examples 1-4.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of Cox et al and Wild et al to modify the IL-4 antagonists taught by Wild et al, by substituting desired amino acid residues with cysteine residues by following the techniques disclosed by Cox et al and generating IL-4 muteins that antagonize IL-4 mediated processes. With respect to claims that recite specific kd concentrations and inhibition of specific cells, the skilled artisan can test the binding efficiency of the modified IL-4 produced by the combined methods of Cox and Wild and can also test whether said modified IL-4 mutiens inhibit the proliferation of any IL-4 stimulated cells. Although the Wild et al reference does not teach specific mutations at positions 37, 104, it teaches that modifying amino acid residues 38 and 105 results in an IL-4 antagonists that antagonize IL-4 activity. Therefore, one skilled in the art would be motivated to modify this region of IL-4 to generate an active IL-4 antagonists because of the teachings of Wild et al with great expectation of success. The skilled artisan would also be motivated to substitute amino acids in this region with a cystiene residue, because Cox et al teach the advantage of doing so. The person of ordinary skill in the art would have been motivated to make the modification in view of Cox et al disclosure by covalently coupling a polymer via the cysteine residue, in order to obtain IL-4 antagonists that retain the desired activity with prolonged circulating half-life. Accordingly, the invention, taken as a whole, is prima facie obvious over the cited prior art.

Conclusion:

4. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday-Thursday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
17 July 2007

EILEEN B. O'HARA
PRIMARY EXAMINER